End-Stage Renal Disease Due to Multiple Myeloma in the United States, 2000-2010.

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Scott Arnold Reule

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Areef Ishani, MD., MS.

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Abstract.

While the management of myeloma and light chain deposition disease ("MM") has changed considerably in the last decade, it is unknown how the burden of associated end-stage renal (ESRD) has evolved.

Methods.

United States Renal Data System data (*n* = 1,048,683) for the years 2001-2010 were used to calculate incidence rates and outcomes of MM (*n* = 12,704, 1.3%).

Results.

Compared to 2001-2002, standardized incidence ratios declined to 0.8 for 2009-2010. Characteristics of MM patients included older age (≥ 65, 63.7% vs. 43.7%) and white race (76.3% vs. 65.1%). Multiple myeloma was associated with a greater likelihood of death (adjusted hazards ratio [AHR] 2.3) and a lower likelihood of listing for (AHR 0.2) a kidney transplant. While hazards ratios for listing increased over time (AHR 1.06 for 2009-2010 Vs. 2001-2002), those for transplant and death did not (AHRs 0.6 and 0.9, respectively). Regional variation in outcomes was apparent, as patients in the South were more likely to die (AHR 1.04 Vs. the Northeast), and more likely to not be listed (AHR 2.4) nor receive a transplant (AHR 2.9).

Conclusions.

While ESRD due to MM has declined in the United States, outcomes on dialysis remain poor and exhibit substantial geographic variation.

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MM – multiple myeloma.

ESRD - end stage renal disease.

US – United States.

SIR – standardized incidence ratio.

AOR – adjusted odds ratio.

GFR – glomerular filtration rate.

BMI – body mass index.

g/dL – gram per deciliter.

Hgb – hemoglobin.

AHR – adjusted hazards ratios.

USRDS – United States Renal Data System.

CMS – Centers for Medicare and Medicaid services.

Medevid05 – Medical Evidence Report (form 2728), 2005.

Medevid95 – Medical Evidence Report (form 2728), 1995.

Waitlist_ki – kidney transplant wait list file.

Waitlist_kp – kidney and pancreas wait list file

Introduction.

Multiple myeloma and light chain deposition disease (collectively referred to as "MM") belong to a family of plasma cell dyscrasias associated with significant renal involvement; having been reported to be the most common malignancy leading to ESRD[1]. Reduction in production of light chains is the hallmark of therapy (related to renal recovery) and even in the setting of aggressive therapy, there is a high rate of progression to ESRD, with recovery occurring in only 15 – 20% of patients[2]. Kidney disease is a common feature of MM with ominous prognostic implications[3, 4]. Novel treatments such as lenalidomide, thalidomide, bortezomib, and use of autologous stem cell transplantation offer hope and survival prospects for patients with MM have improved in recent years[5-11]. In contrast, it is unknown how the burden of ESRD due to MM has evolved. Hence, we sought to describe the clinical and epidemiologic trends of ESRD due to MM in the US from 2000-2010.

Results.

The overall incidence rate of dialysis requiring ESRD (Table 1, Figure 1) due to MM was 4.5 per million in 2001-2002. This rate remained largely unchanged until later biennia, significantly decreasing in 2007-2008 (4.1) and further decreased in 2009-2010 (3.9). In each biennium, higher incidence rates were associated with older age, male gender, African American race, and residence in both the Northeast and Midwest. Standardized incidence ratios (SIR) decreased over time, both in the overall population (SIR 0.8 for 2009-2010 vs. 2001-2002) and in all subgroups examined except those < 45 years old, Hispanic ethnicity, and residence in the West.

Table 2 compares characteristics of patients initiating maintenance dialysis therapy due to MM versus non-MM causing ESRD. Associations with AOR >1.5 (adjusted for age, sex, race/ethnicity) included age 40-64 years (AOR 5.13), age 65 years or older (AOR 6.95), white race (AOR 1.58), presence of graft (AOR 1.66) or catheter (AOR 4.61) at dialysis initiation, and pre-dialysis nephrology care of < 12 months (AOR 3.18). Characteristics associated with an AOR < 0.66 (the reciprocal of 1.5) include Hispanic ethnicity (0.42), ischemic heart disease (AOR 0.39) and diabetes mellitus (AOR 0.2), peritoneal dialysis (AOR 0.47), GFR > 15 ml/min/1.73m^2 (AOR 0.4), BMI > 30 kg/m^2 (AOR 0.52), and a higher serum hemoglobin (AOR 0.61; 9-10.9 g/dL, AOR 0.38; ≥ 11 g/dL).

Figure 2 demonstrates outcomes rates in subjects with ESRD due to MM compared to those remaining with ESRD, matched for age, sex, race/ethnicity, and year of dialysis initiation. Mortality rates were higher in all subgroups of patients with MM (overall rate of 58.1 vs. 25.8, ratio 2.25). Ratios were similar across most subgroups, with the highest ratio observed in those < 40 years (AOR 3.38). Similar mortality rates were seen in the 5 biennia. Subjects with MM were 4.5 times less likely to be listed for kidney transplantation and 4.3 times less likely to receive a transplant, with the least likelihood of both listing (AOR 0.07) and receipt of transplant (AOR 0.1) observed in 2009-2010. Likelihood of listing for transplant appeared to decrease over time, with the lowest regional rates of transplant listing and receipt of kidney transplant associated with regional residence in both the West (AOR 0.19 for listing; AOR 0.18 for transplant received) and the South (AOR 0.15 for listing; AOR 0.125 for transplant received).

Outcomes among patients with ESRD due to MM are shown in Table 3. The highest risk ratios (AOR > 1.5) for mortality were observed in age 40 – 64 years (AHR 2.15 vs. age < 40 years), age ≥ 65 years (AHR 3.92), use of catheter (AHR 2.12 Vs. fistula), and serum albumin < 3.5 g/dL (1.57 vs. albumin > 4 g/dL). Likelihood of listing decreased with age (AHR 0.27, 40-64 yrs; AHR 0.05, > 65 yrs), catheter use (AHR 0.29), dialysis ≤ 12 months (AHR 0.35) and residence in the South (AHR 0.42). Factors associated with increased likelihood of listing include peritoneal dialysis (AHR 2.63) and increasing serum hemoglobin levels (AHR 1.74, Hgb 9-10.9g/dL; AHR 2.34, Hgb ≥ 11 g/dL). Characteristics associated with increased likelihood of transplantation largely paralleled that of listing for transplantation peritoneal dialysis (AHR 2.13), and hemoglobin ≥ 11 g/dL (AHR 2.41). Those associated with decreased likelihood of transplantation included increasing age (AHR 0.29, 40-64 years; AHR 0.04, ≥ 65 years), catheter (AHR 0.26), dialysis duration ≤ 12 months (AHR 0.35), and residence in the South and West regions (AHR 0.35 and AHR 0.52, respectively).

Approximately 1.5% of patients with ESRD due to MM underwent listing for transplantation and only 0.9% (*n* = 109) received transplant; 61.5% were male, 83.5% were white, 84% had been on dialysis > 12 months, and 59.4% received live donor transplants (Table 4). Over time, the number of total transplants performed increased, nearly doubling by 2009-2010 (23.9% Vs. 11.9%). Graft loss and death after 1 year occurred in 4.6% and 6.4%, respectively. Graft loss occurred in 13.8% and death in 20.2% of those transplanted with MM. Approximately 41.7% of the transplants occurred with residence in the Midwest and 25.9% occurred in the Northeast.

Methods.

The main objectives of this study were to describe trends in biannual incidence rates between 2001 and 2010, the main objective, with and without considering trends in the demographic characteristics of the US population, determine incidence rate trends in subgroups of the US population defined by age, sex, and race/ethnicity, and determine rates and risk factors for the following clinical outcomes occurring after initiation of maintenance dialysis for ESRD from MM: death, wait-listing for kidney transplant, and receipt of kidney transplant.

This was a retrospective study using United States Renal Data System (USRDS) standard analysis files to study US patients who initiated dialysis between 2001 and 2010 (n = 1,048,683). Patient characteristics at initiation of were obtained from the USRDS Medical Evidence Report (Centers for Medicare & Medicaid [CMS] form CMS-2728, with corresponding data in the Medevid95 and Medevid05 files). This form changed in 2005; additional data fields gather information about vascular access used at hemodialysis initiation and duration of pre dialysis nephrology care. Of note, the options for designating primary cause of ESRD remained unchanged. Cases of MM and LCDD for this study listed primary cause of ESRD as "multiple myeloma" and "light chain deposition disease". Dates of death and first kidney transplant were obtained from the Patients file, and first listing for renal transplant from the Waitlist_ki and Waitlist_kp files. US census data were used to determine general population denominators for each year studied, with age in 5-year increments and race/ethnicity classified as non-Hispanic white, non-Hispanic black, Hispanic, and other. The Poisson distribution was used to calculate incidence rates.

For the calculation of standardized incidence ratios, expected incidence rates were calculated by applying incidence rates in 2000 for each of the possible combinations of age (21 subgroups), sex (2 subgroups), and race-ethnicity (4 subgroups) to the corresponding subgroup of the US population for each year 2001 to 2010. Chi-square analysis and logistic regression, respectively, were used for comparisons of patients with and without MM at dialysis initiation. Cox regression was used to calculate hazards ratios for outcomes after initiation of dialysis, with follow-up extending to June 30, 2011. Graphical comparison of survival among patients with and without MM was performed after matching each MM patient with a non-MM patient according to the following variables: year and quarter of dialysis initiation, age (in 1-year increments), sex, race, and ethnicity. SAS, v9.1.3 (Cary, North Carolina) was used for data analysis.

Discussion.

While European studies have demonstrated an increase in incidence of ESRD due to MM of 0.7 to 2.52 per million people from 1986 to 2005, we have shown a significant decrease in the standardized incidence rates and ratios of patients initiating dialysis due to MM in the US, particularly in the last two biennia of the observation[13]. The majority of cases occurred in those aged ≥ 65 years and reduced incidence ratios were seen in nearly all subgroups examined with few exceptions. Given that most patients with MM are diagnosed at age > 65 years or older, we demonstrate a positive association of age with mortality, with its greatest effect in those ≥ 65 years (AHR 3.92)[14]. There appeared to be no change with residence in the West and a possible increase in those patients < 45 years of age, fewer women reaching ESRD in recent years (2006-2010 vs. 2001-2005; 41.4%

vs. 46.2%) and an overall increase in those initiating dialysis at a GFR > 15 ml/min^2 (4.3% vs. 7.2%). As expected, overall incidence rates of disease remained lowest in the youngest subgroup of patients.

Those whom were transplanted were more likely to be from the most earlier biennia, utilize a fistula for dialysis, be under the care of a Nephrologist > 12 months, and less likely to be from a Southern region. These effects likely reflected combination of access and care delivery, as well as a possible performance status effect yielding differing treatments[15]. As this analysis was limited in its ability to detect whether these findings are directly related to advances in therapy such as changes in standard chemotherapeutic protocols, introduction of proteasome inhibitors, and variable dialysis as modalities, providers should be cautiously optimistic.[10, 11, 16-18].

Transplantation in the setting of MM is an area with surprisingly few studies and remains a controversial topic given the nature and survival with disease, recurrence, and risk of adverse outcome. In one series of 9 patients with myeloma cast nephropathy, survival reports yielded a wide range of 14 to 114 months[19]. We demonstrate that only 0.9% (n = 109) of patients in our analysis underwent transplantation over the 10-year follow up period, a number slightly lower than the 1.4% observed in European registries[20]. Previous experience has demonstrated that approximately 30% of kidney transplants performed in the setting of MM were received from a live donor, whereas 60% of transplants were received from a living donor in our analysis[13]. We found that mortality remained significantly higher (AHR 2.25) and transplant listing rates were lower in patients with ESRD due to MM in comparison to age-, race- and gender-matched controls in nearly all subgroups. Our findings demonstrate similar graft survival

between groups at one year (MM versus remaining ESRD; 11.4% vs. 13.6%), however death occurred in nearly twice as many patients (20.2% vs. 11.8%).

There several important limitations to our study, many of which arise from use of retrospective registry-based data, lack of definitive pathology, and variables with known prognostic implications, including free light chain and β_2 microglobulin level[21, 22]. Additional clinical information such as performance status and intensity of chemotherapy, are not known. Regardless, there are a number of strengths including the use of the large size and representative population of interest. This study provides important insight in to the landscape and care delivery afforded to patients with ESRD. Future studies lie within the identification of clinical parameters and patient variables that help clinicians stratify patients whom are appropriate for transplantation.

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Competing Financial Interests.

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Table 1. Incidence Rates and Standardized Incidence Ratios of Dialysis-Requiring ESRD Due to MM and Other Causes in the US, 2001-2010.

	Biennium				
	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010
	Population Size, Mean				
	286,297,074	291,456,616	296,948,256	302,662,587	308,060,609
	Cases				
	2,558	2,518	2,696	2,511	2,421
	Incidence Rate, Per Million Per Year				
All	4.5 (0.1)[a]	4.3 (0.1)[a]	4.5 (0.1)[a]	4.1 (0.1)[a]	3.9 (0.1)[b]
Age, years					
0-44	0.2 (0)[a]	0.2 (0)[a]	0.3 (0)[a]	0.2 (0)[a]	0.2 (0)[a]
45-64	5.8 (0.2)[a]	6 (0.2)[a]	6.2 (0.2)[a]	5.4 (0.2)[a]	5.2 (0.2)[a]
≥ 65	24.3 (0.6)[a]	22.4 (0.6)[a]	22.7 (0.6)[a]	20.6 (0.5)[c]	18.7 (0.5)[c]
Sex					
Male	4.8 (0.1)[a]	4.7 (0.1)[a]	5.2 (0.1)[a]	5 (0.1)[a]	4.7 (0.1)[a]
Female	4.1 (0.1)[a]	4 (0.1)[a]	3.9 (0.1)[a]	3.3 (0.1)[c]	3.2 (0.1)[c]
Race/Ethnicity					
Non-Hispanic white	4.7 (0.1)[a]	4.6 (0.1)[a]	4.9 (0.1)[a]	4.4 (0.1)[a]	4.2 (0.1)[a]
Non-Hispanic black	7.3 (0.3)[a]	7.2 (0.3)[a]	7.7 (0.3)[a]	6.8 (0.3)[a]	6.8 (0.3)[a]
Hispanic	1.7 (0.1)[a]	1.8 (0.1)[a]	2 (0.2)[a]	2 (0.1)[a]	1.7 (0.1)[a]
Other	1.9 (0.2)[a]	1.8 (0.2)[a]	1.2 (0.2)[a]	1.7 (0.2)[a]	1.5 (0.2)[a]
Region					
Northeast	6.9 (0.3)	6.7 (0.3)	6.7 (0.3)	6 (0.3)	5.7 (0.3)[a]
Midwest	5.3 (0.2)	4.5 (0.2)	5 (0.2)	5.2 (0.2)	4.6 (0.2)
South	4.3 (0.1)	4.4 (0.1)	4.7 (0.1)	4 (0.1)	3.8 (0.1)
West	4.2 (0.2)	4.5 (0.2)	4.6 (0.2)	4.4 (0.2)	4.3 (0.2)
	Standardized Incidence Ratios				
All	1 (Ref)	0.95 (0.02)	0.98 (0.02)	0.87 (0.02)00	0.8 (0.02)00
Age,years					
0-44	1 (Ref)	0.92 (0.11)	1.44 (0.14)	1.24 (0.13)	1.15 (0.13)
45-64	1 (Ref)	1.01 (0.04)	1.03 (0.03)	0.89 (0.03)	0.83 (0.03)[b]
≥ 65	1 (Ref)	0.92 (0.02)	0.93 (0.02)	0.85 (0.02)[b]	0.78 (0.02)[c]
Sex					
Male	1 (Ref)	0.94 (0.03)	1.03 (0.03)	0.97 (0.02)	0.87 (0.02)[b]
Female	1 (Ref)	0.96 (0.03)	0.92 (0.03)	0.76 (0.02)[c]	0.72 (0.02)[c]
Race/Ethnicity					
Non-Hispanic white	1 (Ref)	0.94 (0.02)	0.98 (0.02)	0.87 (0.02)[b]	0.8 (0.02)[c]
Non-Hispanic black	1 (Ref)	0.96 (0.04)	1 (0.04)	0.84 (0.04)[a]	0.81 (0.04)[a]

Hispanic	1 (Ref)	1.05 (0.09)	1.13 (0.09)	1.1 (0.08)	0.9 (0.07)
Other	1 (Ref)	0.93 (0.11)	0.59 (0.09)[a]	0.83 (0.1)	0.68 (0.08)
Region					
Northeast	1 (Ref)	0.97 (0.04)	0.97 (0.04)	0.84 (0.04)[a]	0.78 (0.03)[b]
Midwest	1 (Ref)	0.85 (0.04)[a]	0.92 (0.04)	0.92 (0.04)	0.78 (0.03)[b]
South	1 (Ref)	1.02 (0.03)	1.06 (0.03)	0.89 (0.03)	0.82 (0.03)[b]
West	1 (Ref)	1.1 (0.05)	1.12 (0.05)	1.03 (0.05)	0.98 (0.05)

Note: Parameter estimates are reported with standard errors in parentheses. Standardized incidence ratios were calculated by applying rates for 2001-2002 to other biennia. $P \geq 0.05$ unless otherwise indicated.

[a] $0.01 \leq P$ value (vs. 2000) < 0.05.

[b] $0.001 \leq P$ value (vs. 2000) < 0.01.

[c] P value (vs. 2000) ≤ 0.001.

Table 2. Baseline Characteristics of Subjects at Initiation of Maintenance Dialysis due Multiple Myeloma.

		All Patients (*n* = 1,048,683)			Patients with MM or LCDD (*n* = 12,704)
		MM or LCDD	No MM or LCDD	AOR MM or LCDD	AOR 2006-2010 Vs. 2001-2005
n		12,704	1,035,979		
Renal Disease	Multiple Myeloma	100	0		
	Diabetes	0	45.8		
	Hypertension	0	28.5		
	Other	0	25.7		
Year of first dialysis	2001-2002	20.1	18.4	1(Ref)	
	2003-2004	19.8	19.3	0.94 (0.89-1)	
	2005-2006	21.2	20.2	0.96 (0.91-1.01)	
	2007-2008	19.8	20.7	0.88 (0.83-0.93)	
	2009-2010	19.1	21.5	0.82 (0.77-0.86)	
Age, yrs.	< 40	1.4	8.9	1(Ref)	1(Ref)
	40-64	35	41.5	5.13 (4.41-5.98)	0.69 (0.51-0.95)
	≥ 65	63.6	49.6	6.95 (5.97-8.09)	0.63 (0.46-0.86)
Female Sex	Vs. Male	43.8	44.5	0.98 (0.95-1.02)	0.82 (0.77-0.88)
Race	White	76.4	65.1	1(Ref)	1(Ref)[a]
	Black	20.8	28.9	0.63 (0.61-0.66)	1.06 (0.97-1.15)
	Other	2.8	6	0.42 (0.38-0.47)	0.96 (0.78-1.19)
Hispanic ethnicity	Yes Vs. No	6.4	13.6	0.42 (0.39-0.46)	1.35 (1.17-1.56)
Ischemic Heart Disease	Yes Vs. No	13.9	24	0.39 (0.37-0.41)	0.86 (0.77-0.95)
Diabetes	Yes Vs. No	17.5	52.9	0.2 (0.19-0.21)	1.26 (1.15-1.38)
Peritoneal Dialysis	Vs. Hemodialysis	3.1	6.8	0.47 (0.43-0.52)	0.77 (0.63-0.95)
Hemodialysis access	Fistula	3.6	13.9	1(Ref)	1(Ref)[a]
	Graft	1.5	3.6	1.66 (1.32-2.09)	0.53 (0.28-1.03)
	Catheter	94.9	82.4	4.61 (4.07-5.23)	0.81 (0.53-1.23)
Prior nephrology care ≤ 12 mo.	Vs. > 12 mo.	90.4	76.3	3.18 (2.94-3.44)	0.84 (0.65-1.08)
GFR > 15 ml/min/1.73	Vs. ≤ 15	5.7	12.3	0.4 (0.37-0.43)	1.67 (1.43-1.96)

m^2					
Body mass index, kg/m^2	18.5-24.9	42.6	33.4	1(Ref)	1(Ref)
	< 18.5	5	4.3	0.94 (0.86-1.02)	0.8 (0.67-0.95)
	25-29.9	31.1	28.4	0.87 (0.83-0.9)	1.15 (1.06-1.25)
	≥ 30	21.3	33.8	0.52 (0.5-0.55)	1.55 (1.41-1.7)
Albumin, g/dL	≥ 4.0	10.4	11.6	1(Ref)	1(Ref)[a]
	3.5-3.9	18.4	22.4	0.88 (0.81-0.95)	1.02 (0.87-1.19)
	< 3.5	71.2	66.1	1.2 (1.12-1.28)	0.92 (0.8-1.05)
Hemoglobin, g/dL	< 9	36.3	26	1(Ref)	1(Ref)
	9-10.9	46.7	47.2	0.61 (0.59-0.64)	1.01 (0.93-1.09)
	≥ 11	17	26.8	0.38 (0.36-0.4)	0.7 (0.63-0.78)
Region	Northeast	22.2	17.9	1(Ref)	1(Ref)[a]
	Midwest	23.5	21.6	0.86 (0.82-0.91)	1.13 (1.02-1.26)
	South	36	40.4	0.83 (0.79-0.87)	1.07 (0.97-1.18)
	West	18.2	20.1	0.9 (0.85-0.95)	1.1 (0.99-1.24)

Note: Parameter estimates are presented as column percentages or odds ratios, with 95% confidence intervals in parentheses. Reflecting the fact that 2005 was the first complete year in which data fields for pre dialysis vascular access for hemodialysis and pre dialysis nephrology care were included in the Medical Evidence Report, the denominators for these variables consisted of patients initiating dialysis 2005-2010.

$P < 0.05$ for statistical comparisons, unless otherwise indicated.

Missing data were as follows: GFR, n =0.6%; BMI, n = 1.4%; Hemoglobin, n = 8.4%; Albumin, n = 24.7%, Region n = 1.8%

BMI, body mass index; GFR, glomerular filtration rate.

[a]$P \geq 0.05$.

Table 3. Outcomes According to Presence or Absence of Multiple Myeloma (n = 1,048,683)

		All Patients (n = 1,048,683)					
		Death 57.8 (23.6 at 1 Year)		Transplant Listing 17.3 (10.5 at 1 Year)		Transplanted 9 (2.6 at 1 Year)	
	Characteristics	Rate	AHR, Death	Rate	AHR, Listing	Rate	AHR, Non-Transplant
Multiple Myeloma	No	19.7 (0)	1 (Ref)	6.5 (0)	1 (Ref)	3.5 (0)	1 (Ref)
	Yes	57.9 (0.6)	2.3 (2.3-2.4)	1 (0.1)	0.2 (0.2-0.2)	0.6 (0.1)	0.2 (0.2-0.2)
		Patients with MM (n = 12,704)					
		Death 82.9 (55.8 at 1 year)		Transplant Listing 1.5 (0.5 at 1 Year)		Transplanted 0.9 (0.1 at 1 Year)	
	Characteristics	Rate	AHR, Death	Rate	AHR, Listing	Rate	AHR, Transplant
Year of first dialysis	2001-2002	58.2 (1.2)	1 (Ref)	0.6 (0.1)	1 (Ref)	0.5 (0.1)	1 (Ref)
	2003-2004	59.6 (1.2)[a]	1.04 (0.99-1.1)[a]	1.2 (0.2)[b]	1.75 (1.08-2.84)[b]	0.8 (0.1)[a]	1.43 (0.82-2.47)[a]
	2005-2006	54.6 (1.1)[b]	0.95 (0.9-1.01)[a]	1.2 (0.2)[b]	1.75 (1.08-2.82)[b]	0.8 (0.1)[a]	1.36 (0.79-2.33)[a]
	2007-2008	56.6 (1.3)[a]	0.97 (0.91-1.02)[a]	1.2 (0.2)[b]	1.77 (1.08-2.9)[b]	0.5 (0.1)[a]	0.87 (0.46-1.65)[a]
	2009-2010	63.4 (1.7)[b]	1.06 (0.99-1.13)[a]	0.6 (0.2)[a]	0.91 (0.46-1.81)[a]	0.3 (0.1)[a]	0.54 (0.22-1.34)[a]
Age, yrs.	< 40	18.6 (2)	1 (Ref)	5.8 (1.2)	1 (Ref)	3.2 (0.9)	1 (Ref)
	40-64	40.8 (0.7)	2.15 (1.74-2.65)	1.5 (0.1)	0.27 (0.17-0.42)	1 (0.1)	0.29 (0.16-0.51)
	≥ 65	74.8 (0.9)	3.92 (3.19-4.83)	0.3 (0.1)	0.05 (0.03-0.09)	0.2 (0.1)	0.04 (0.02-0.09)
Female sex	Vs. Male	57.1 (0.8)[a]	0.97 (0.93-1)[a]	0.8 (0.1)[b]	0.78 (0.57-1.06)[a]	0.5 (0.1)[a]	0.83 (0.56-1.22)[a]
Race	White	54.7 (1.2)	1 (Ref)	0.7 (0.1)	1 (Ref)	0.4 (0.1)	1 (Ref)
	Black	59.5 (0.6)	1.04 (0.99-1.09)[a]	1 (0.1)[b]	0.7 (0.37-1.34)[a]	0.7 (0.1)[b]	1.26 (0.46-3.44)[a]
	Other	43.8 (2.6)	0.8 (0.7-0.9)	1.6 (0.6)[b]	0.42 (0.2-0.87)[b]	0.6 (0.4)[a]	0.55 (0.18-1.67)[a]
Hispanic Ethnicity	Yes Vs. No	49.3 (2)	0.92 (0.85-1)[a]	1.9 (0.4)	1.43 (0.91-2.24)[a]	0.6 (0.3)[a]	0.66 (0.32-1.38)[a]
Ischemic heart disease	Yes Vs. No	73.1 (1.9)	1.11 (1.05-1.17)	0.4 (0.2)[b]	0.68 (0.34-1.34)[a]	0.2 (0.1)[b]	0.46 (0.17-1.27)[a]
Diabetes	Yes Vs. No	66.7 (1.6)	1.13 (1.08-1.19)	0.6 (0.2)[b]	0.68 (0.41-1.13)[a]	0.4 (0.1)[a]	0.68 (0.35-1.3)[a]

Peritoneal Dialysis	Vs. Hemodialysis	39.6 (2.3)	0.69 (0.61-0.77)	2.7 (0.6)	2.63 (1.62-4.27)	1.5 (0.5)[c]	2.13 (1.13-4)[b]
Access	Fistula	30.8 (2.6)	1 (Ref)	2.5 (0.8)	1 (Ref)	1.3 (0.6)	1 (Ref)
	Graft	45.9 (5.2)[c]	1.45 (1.1-1.91)[c]	1.9 (1.3)[a]	0.96 (0.26-3.49)[a]	0.6 (1)[a]	0.53 (0.06-4.46)[a]
	Catheter	60.1 (0.8)	2.12 (1.8-2.5)	0.9 (0.1)[c]	0.29 (0.15-0.55)	0.5 (0.1)[b]	0.26 (0.11-0.62)[c]
Prior nephrology care ≤ 12 mo.	Vs. > 12 mo.	58.8 (0.8)	1.38 (1.25-1.52)	1 (0.1)[c]	0.35 (0.21-0.6)	0.5 (0.1)[b]	0.35 (0.17-0.71)[c]
GFR > 15 mL/min/1.73 m^2	Vs. ≤ 15	61 (2.5)[a]	1.07 (0.98-1.16)[a]	0.7 (0.3)[a]	0.72 (0.34-1.53)[a]	0.2 (0.2)[a]	0.32 (0.08-1.28)[a]
BMI, kg/m^2	18.5-24.9	62.3 (0.9)	1 (Ref)	0.9 (0.1)	1 (Ref)	0.6 (0.1)	1 (Ref)
	< 18.5	75.4 (3.2)	1.2 (1.1-1.31)	1 (0.4)[a]	1.25 (0.57-2.74)[a]	0.3 (0.3)[a]	0.51 (0.12-2.12)[a]
	25-29.9	54.7 (1)	0.9 (0.86-0.94)	0.9 (0.1)[a]	0.87 (0.6-1.26)[a]	0.6 (0.1)[a]	0.93 (0.59-1.46)[a]
	≥ 30	51.5 (1.1)	0.89 (0.85-0.94)	1.2 (0.2)[a]	1.17 (0.8-1.71)[a]	0.7 (0.1)[a]	1.08 (0.67-1.75)[a]
Albumin, g/dL	≥ 4	37.9 (1.4)	1 (Ref)	1.6 (0.3)	1 (Ref)	0.8 (0.2)	1 (Ref)
	3.5-3.9	48.9 (1.3)	1.21 (1.11-1.32)	1.3 (0.2)[a]	0.93 (0.56-1.52)[a]	0.9 (0.2)[a]	1.32 (0.7-2.46)[a]
	< 3.5	64.7 (0.8)	1.57 (1.45-1.69)	0.8 (0.1)[c]	0.66 (0.43-1.01)[a]	0.5 (0.1)[b]	0.71 (0.4-1.26)[a]
Hemoglobin, g/dL	< 9	64 (1.1)	1 (Ref)	0.7 (0.1)	1 (Ref)	0.5 (0.1)	1 (Ref)
	9-10.9	58 (0.9)	0.86 (0.83-0.9)	1 (0.1)[b]	1.74 (1.17-2.59)[c]	0.6 (0.1)[a]	1.49 (0.92-2.43)[a]
	≥ 11	48.3 (1.2)	0.71 (0.67-0.75)	1.4 (0.2)	2.34 (1.51-3.64)	1 (0.2)[c]	2.41 (1.42-4.08)[c]
Region	Northeast	61.2 (1.3)	1 (Ref)	1.2 (0.2)	1 (Ref)	0.8 (0.2)	1 (Ref)
	Midwest	54.4 (1.1)	0.9 (0.85-0.96)	1.2 (0.2)[a]	0.97 (0.65-1.46)[a]	1 (0.2)[a]	1.21 (0.75-1.96)[a]
	South	59.2 (0.9)[a]	1.02 (0.97-1.08)[a]	0.6 (0.1)	0.42 (0.27-0.65)	0.3 (0.1)[c]	0.35 (0.19-0.63)
	West	56.3 (1.3)[c]	0.98 (0.92-1.04)[a]	1.1 (0.2)[a]	0.75 (0.48-1.16)[a]	0.5 (0.1)[a]	0.52 (0.28-0.98)[b]

Parameter estimates are presented with either standard errors or 95% confidence intervals in parentheses. Rates are expressed per 100 person-years. Hazards ratios for non-occurrence of listing and transplant were calculated as the inverse of the corresponding estimate for event occurrence. P values < 0.001 unless otherwise stated. AHR, adjusted (for age, sex, race, ethnicity) hazards ratio; BMI, body mass index; GFR, glomerular filtration rate; MM, Multiple Myeloma. [a] *P* value ≥ 0.05; [b] 0.01 ≤ *P* value < 0.05; [c] 0.001 ≤ *P* value < 0.01

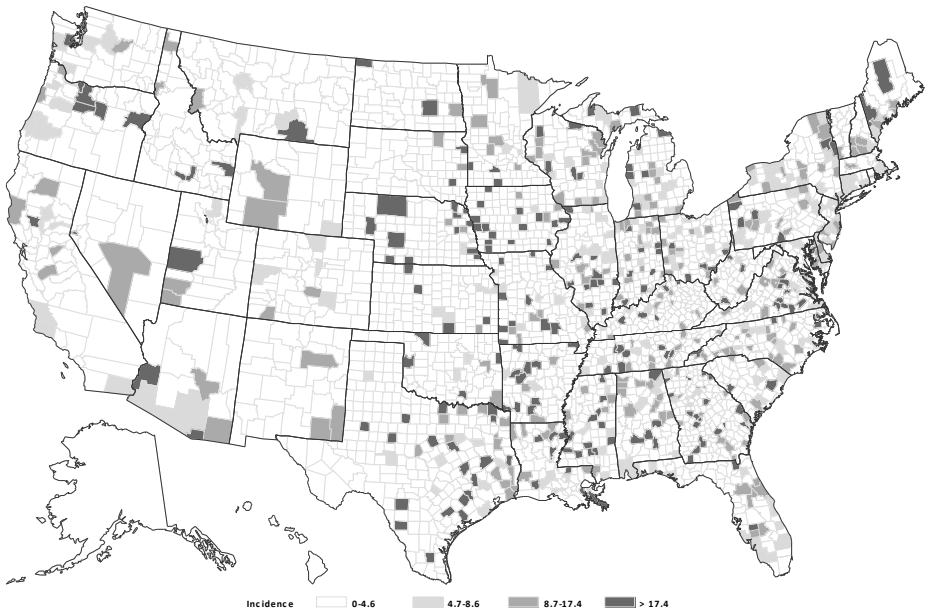
Table 4. Event Ratios for Death and Graft Loss in Patients with MM (*n* =109).

	Characteristics at Transplant (%)		Outcomes After Transplant (%)		
Transplant Year	2001-02	11.9	Graft loss	%	13.8
	2003-04	10.1		% at 1 yr.	4.6
	2005-06	27.5		Rate	4.2 (1.2)[a]
	2007-08	26.6		AHR (Vs. Non MM)	1.6 (1-2.7)[a]
	2009-10	23.9	Death	%	20.2
Donor	Living	59.6		% at 1 yr.	6.4
	Deceased	40.4		Rate	6.1 (1.4)[c]
	≤ 1	16.5		AHR (Vs. Non MM)	1.6 (1-2.4)[b]
Years on dialysis					
	> 1	83.5	Graft loss or death	%	26.2
Age at transplant, yrs.	< 40	9.2		% at 1 yr.	10.1
	40-64	73.4		Rate	8.4 (1.6)[b]
	≥ 65	17.4		AHR (Vs. Non MM)	1.6 (1-2.4)[b]
Female Sex		38.5			
Race	Black	12.8			
	White	83.5			
	Other	3.7			
Hispanic ethnicity		7.3			
Ischemic heart disease		3.7			
Diabetes		9.2			
Region	Northeast	25.9			
	Midwest	41.7			
	South	17.6			
	West	14.8			

Note: Parameter estimates are presented with standard errors or 95% confidence intervals in parentheses. Rates are expressed per 100 person-years. *P* values ≥ 0.05 throughout.

AHR, adjusted (for age, sex, race, ethnicity) hazards ratio; BMI, body mass index; GFR, glomerular filtration rate; MM, multiple myeloma or light chain deposition disease.

Figure 1. County-level incidence rates, per million, of dialysis-requiring patients with Multiple Myeloma in 2001-2002 (upper panel) and 2009-2010 (lower panel). Incidence rate categories are quartiles of counties with non-zero incidence rates in 2001-2002.



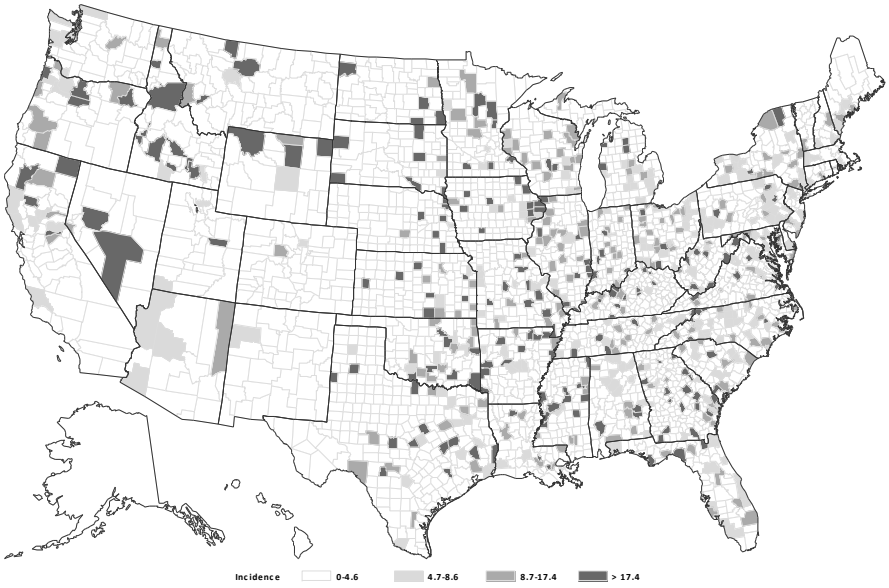
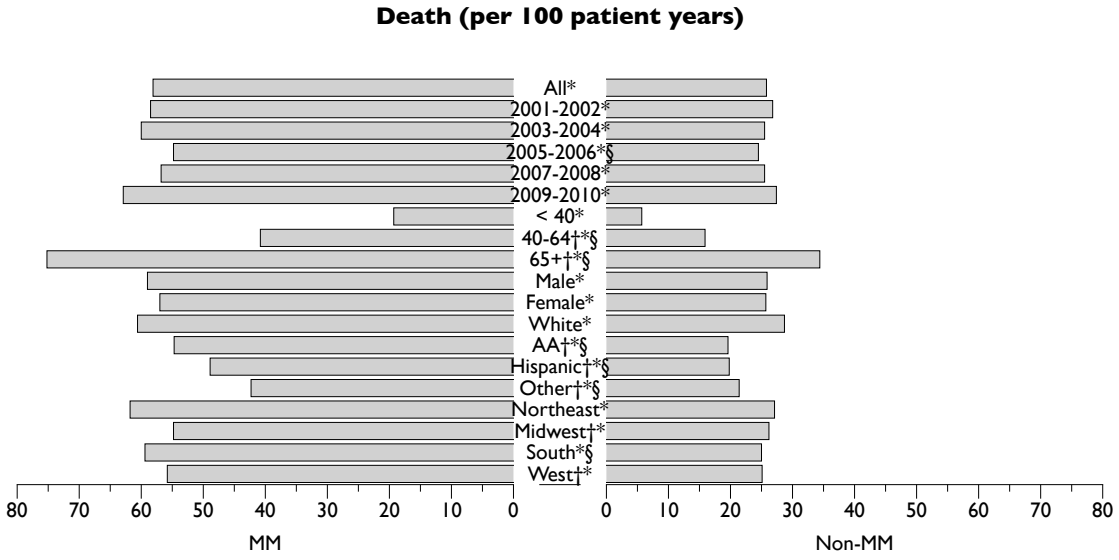
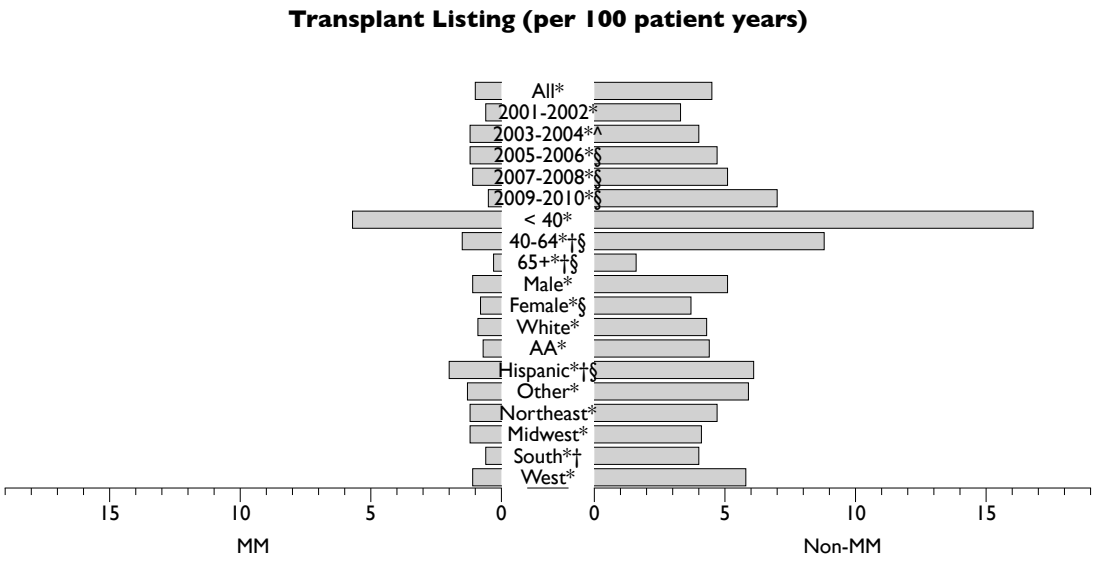
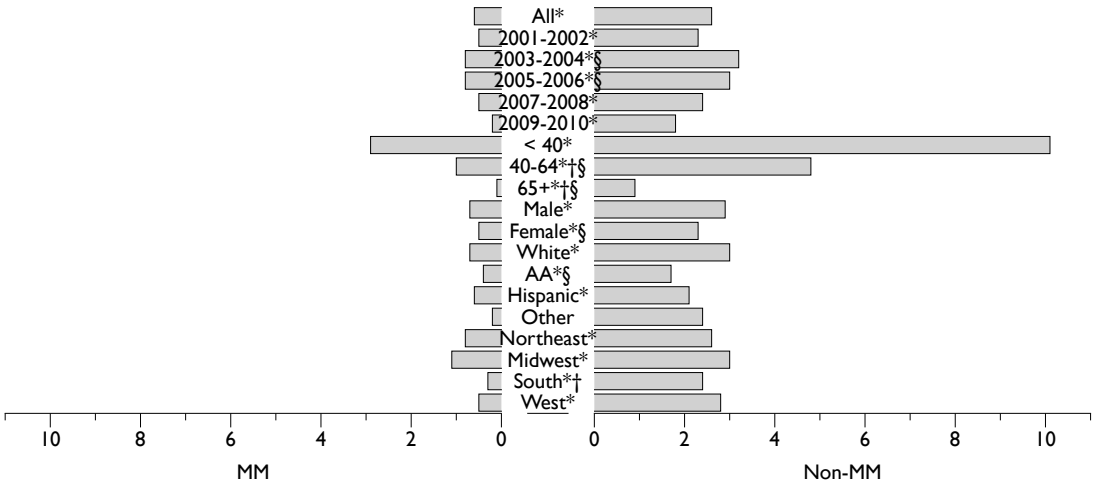


Figure 2. Outcome rates per 100 person-years in patients with Multiple Myeloma (*n* = 12,704, 97.4%) and an equal number of matched control patients without MM. Factors used for matching were: biennium of dialysis initiation (2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010); age (in 5-year increments until 84, ≥ 85); sex (male, female); race/ethnicity (non-Hispanic black, non-Hispanic white, Hispanic, other). Ref groups for statistical comparisons: biennium 2001-2002; age < 40 years; non-Hispanic black race/ethnicity; northeast region.







*$P < 0.05$ for within-subgroup comparison between patients with and without MM.

†$P < 0.05$ for between-subgroup comparison among patients with MM.

§$P < 0.05$ for between-subgroup comparison among patients without MM.

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